REMARKS

The present invention relates to co-repressor polypeptides that are capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors. Exemplary members of the silencing mediators of retinoic acid and thyroid hormone receptors (SMRT) are provided, including various isoforms of human, mouse and Drosophila SMRT co-repressor.

Claims 3-7, 9, 10, 12-14, 16-25 and 38 were pending before this communication. By this response, claims 3-5, 9, 10, 12-14 and 16 have been amended to define Applicant's invention with greater particularity. In addition, claims 6 and 7 have been cancelled without prejudice. For the Examiner's convenience, a marked up version of claims reflecting these amendments is provided herewith as APPENDIX A. These amendments add no new matter as they are fully supported by the specification and original claims

Accordingly, claims 3-5, 9, 10, 12-14, 16-25 and 38 remain pending upon entry of the amendments submitted herewith. For the Examiner's convenience, a clean copy of the complete set of pending claims is provided in APPENDIX B.

With respect to the repeated objection to Figures 5A and 9, replacement sheets for these drawings are provided herewith. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

The rejections of claims 4-6, 9, 12, 14 and 19-22 under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description for the phrase "isoform or peptide portion thereof", is respectfully traversed. As previously argued, Applicants have described the claimed polynucleotide(s) with reference to both structure and function. The claimed polynucleotides encode a family of co-repressors that mediates transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily, of which SEQ ID Nos: 5, 7 and 9 are representative members. These representative SMRT members are respectively a human SMRT, a mouse alpha SMRT isoform, and a mouse

beta SMRT isoform. Thus, the specification clearly provides written description of SMRT isoforms, and provides exemplary complete amino acid sequences therefor. The SMRT isoforms contemplated are therefore merely alternative members of the SMRT family of proteins, as would be understood by one of skill in the art. Furthermore, specific peptide portions of a SMRT co-repressor of interest are clearly described in the specification at page 9, lines 24 through page 10, line 11.

Therefore, because isoforms are included as members of the SMRT family, claims 4, 5, 9, 12 and 14 have been amended herein to delete the redundant term isoform in efforts to further clarify the claim language. Claim 6 has been cancelled by this response, rendering the rejection moot with respect to claim 6. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 4, 5, 9, 12, 14 and 19-22 under 35 U.S.C. § 112, first paragraph.

The rejection of claims 4, 7, 9 and 12 under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description for the term "conservative variations", is respectfully traversed. As acknowledged by the Examiner, this term is commonly used in the art to represent substitutions encoding amino acids such that the tertiary structure of the protein is not substantially altered (see Office Action, Paper No. 19, at page 6, paragraph 10). The Examiner further acknowledges that the specification provides exemplary conservative substitutions (Id.). Thus, Applicants respectfully submit that the specification satisfies the written description requirement for the use of the term "conservative variations".

However, in efforts to reduce the issues and advance prosecution, claims 4, 9 and 12 have been amended herein to delete the term conservative variations, and claim 7 has been cancelled. The claims as amended refer to sequences "having at least 80% sequence identify with" specific SEQ ID Nos, thus providing even further structural and functional characterization of the claimed polynucleotides. These amendments are fully supported by the specification at page 11, lines 14-18 for amino acid sequences and polypeptides or proteins, and at page 17, lines 6-9 for polynucleotide sequences.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 4, 9 and 12 under 35 U.S.C. § 112, first paragraph.

The rejection of claims 3, 5, 14 and 16 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite due to recitation of the phrase "hybridizes under stringent conditions" or similar hybridization language, is respectfully traversed. However, in efforts to reduce the issues and advance prosecution, claims 3, 5, 14 and 16 have been amended herein to replace the phrase and refer instead to polynucleotides "having at least 80% sequence identity " with corresponding polynucleotides or complementary sequences thereto. These amendments are fully supported by the specification at page 17, lines 6-9. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 3, 5, 14 and 16 under 35 U.S.C. § 112, second paragraph.

The rejection of claims 9, 10 and 12 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the phrase "substantially the same" is not defined in the specification (see the last two lines at page 7 of the Office Action, Paper No. 19). Contrary to the Examiner's assertion, this terminology is expressly defined at page 17, line 30 through page 18, line 14 of Applicant's specification. Applicants respectfully submit that in order to advance prosecution, the use of the phrase was previously removed from claims 9 and 12 in the Amendment filed on September 3, 2002. Upon entry of this prior Amendment pursuant to the request for a CPA, the phrase is no longer present in these claims.

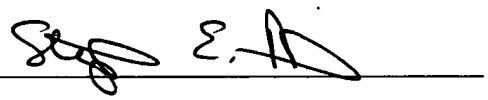
In further efforts to advance prosecution, use of similar language in claims 10 and 13 has been amended herein and replaced with the phrase "having at least 80% sequence identity", consistent with the earlier amendments presented herein. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection of claims 9, 10 and 12, and to the extent that it may apply to prior claim 13, under 35 U.S.C. § 112, second paragraph.

The possibility of a rejection of claims 14 and 16 under 35 U.S.C. § 112, second paragraph, as suggested by the Examiner in the Advisory Action, Paper No. 22, upon entry of the previously unentered amendment, is respectfully traversed. Applicants respectfully submit that the claims are clear as written. However, in order to reduce the issues and advance prosecution, claims 14 and 16 have been amended herein to recite a first and a second polynucleotide to further clarify the claim language. Accordingly, Applicants respectfully request reconsideration and withdrawal of this possible rejection of claims 14 and 16 under 35 U.S.C. § 112, second paragraph.

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this Application can be achieved.

Respectfully submitted,

Date: December 2, 2002

By 

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Enclosures: APPENDICES A & B
Replacement Figures 5A and 9

APPENDIX A – ALTERED CLAIMS

VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Thrice amended) The polynucleotide of claim 4 **[~~and polynucleotides that hybridize thereto under stringent conditions~~]**, wherein the SMRT co-repressor comprises a repression domain having

a) less than about 83% identity with a Sin3A interaction domain of N-CoR set forth as amino acids 255 to 312 of SEQ ID NO: 11;

b) less than about 57% identity with repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11;

c) less than about 66% identity with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11; or

d) less than about 30% identity with repression domain 2 of N-CoR set forth as amino acids 736 to 1031 of SEQ ID NO: 11.

4. (Twice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), **[~~or an isoform~~]** or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein the SMRT co-repressor comprises an amino acid sequence **having at least 80% sequence identity with** [~~as set forth in~~] SEQ ID NO: 5 **[~~or conservative variations thereof~~]**.

5. (Thrice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), **[~~or an isoform~~]** or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said co-repressor is encoded by a

polynucleotide **having at least 80% sequ nce identity** [~~which hybridizes under stringent conditions~~] with SEQ ID NO: 4.

9. (Thrice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), [~~or an isoform~~] or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having **at least 80% sequence identity with** [~~the amino acid sequence set forth in~~] SEQ ID NO: 7 [~~or conservative variations thereof~~].

10. (Thrice amended) The polynucleotide of claim 9, which has a nucleotide sequence **having at least 80% sequence identity with** [~~substantially the same as set forth in~~] SEQ ID NO: 6.

12. (Thrice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), [~~or an isoform~~] or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having **at least 80% sequence identity with** [~~the amino acid sequence set forth in~~] SEQ ID NO: 9 [~~or conservative variations thereof~~].

13. (Twice amended) The polynucleotide of claim 12, which has a nucleotide sequence **having at least 80% sequence identity with** [~~substantially the same as set forth in~~] SEQ ID NO: 8.

14. (Thrice amended) **A first** [~~An~~] isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), [~~or an isoform~~] or **a** peptide portion thereof (collectively, a SMRT co-repressor), or **a second** [~~an~~] isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said **first** polynucleotide **is** [~~comprises a nucleotide sequence having at least 80% sequence identity with a polynucleotide~~] selected from the group consisting of:

(a) **a nucleotide sequence having at least 80% sequence identity with** nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) **a nucleotide sequence having at least 80% sequence identity with** nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) **a nucleotide sequence having at least 80% sequence identity with** nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides **complementary to the sequence of** [~~hybridizing under stringent conditions to~~] (a), (b), or (c),

provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11.

16. (Twice amended) A **first** polynucleotide according to claim 14, wherein said **first** polynucleotide is selected from the group consisting of:

(a) nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides **having at least 80% sequence identity with the complementary sequence of** [~~hybridizing under stringent conditions to~~] (a), (b), or (c).

APPENDIX B - COMPLETE SET OF PENDING CLAIMS

3. (Thrice amended) The polynucleotide of claim 4, wherein the SMRT co-repressor comprises a repression domain having

a) less than about 83% identity with a Sin3A interaction domain of N-CoR set forth as amino acids 255 to 312 of SEQ ID NO: 11;

b) less than about 57% identity with repression domain 1 of N-CoR set forth as amino acids 1 to 312 of SEQ ID NO: 11;

c) less than about 66% identity with a SANT domain of N-CoR set forth as amino acids 312 to 668 of SEQ ID NO: 11; or

d) less than about 30% identity with repression domain 2 of N-CoR set forth as amino acids 736 to 1031 of SEQ ID NO: 11.

4. (Twice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein the SMRT co-repressor comprises an amino acid sequence having at least 80% sequence identity with SEQ ID NO: 5.

5. (Thrice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said co-repressor is encoded by a polynucleotide having at least 80% sequence identity with SEQ ID NO: 4.

9. (Thrice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having at least 80% sequence identity with SEQ ID NO: 7.

10. (Thrice amended) The polynucleotide of claim 9, which has a nucleotide sequence having at least 80% sequence identity with SEQ ID NO: 6.

12. (Thrice amended) An isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or a peptide portion thereof (collectively, a SMRT co-repressor), or an isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said polynucleotide encodes a polypeptide having at least 80% sequence identity with SEQ ID NO: 9.

13. (Twice amended) The polynucleotide of claim 12, which has a nucleotide sequence having at least 80% sequence identity with SEQ ID NO: 8.

14. (Thrice amended) A first isolated polynucleotide encoding a member of a family of silencing mediators of retinoic acid receptor and thyroid hormone receptor (SMRT), or a peptide portion thereof (collectively, a SMRT co-repressor), or a second isolated polynucleotide complementary thereto, wherein said SMRT co-repressor is capable of mediating the transcriptional silencing of at least one member of the steroid/thyroid hormone superfamily of receptors, and wherein said first polynucleotide is selected from the group consisting of:

(a) a nucleotide sequence having at least 80% sequence identity with nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) a nucleotide sequence having at least 80% sequence identity with

nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) a nucleotide sequence having at least 80% sequence identity with nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides complementary to the sequence of (a), (b), or (c),

provided that the polynucleotide does not contain a sequence identical to SEQ ID NO: 11.

16. (Twice amended) A first polynucleotide according to claim 14, wherein said first polynucleotide is selected from the group consisting of:

(a) nucleotides 1 to 3094 of SEQ ID NO: 4;

(b) nucleotides 1 to 3718 of SEQ ID NO: 6;

(c) nucleotides 1 to 2801 of SEQ ID NO: 8; and

(d) polynucleotides having at least 80% sequence identity with the complementary sequence of (a), (b), or (c).

17. (Previously amended) The polynucleotide of claim 10, comprising nucleotides 1 to 8388 of SEQ ID NO: 6.

18. (Previously amended) The polynucleotide of claim 7, comprising nucleotides 1 to 8561 of SEQ ID NO: 4.

19. (Previously amended) The polynucleotide of claim 4, which is operably linked to a second nucleotide sequence.

20. (Reiterated) The polynucleotide of claim 19, which encodes a fusion polypeptide comprising the SMRT co-repressor operably linked to a DNA binding domain of a transcription factor.

21. (Previously amended) A vector comprising the polynucleotide of claim 4.

22. (Previously amended) A host cell containing the polynucleotide of claim 4.

23. (Previously twice amended) An isolated oligonucleotide, comprising at least 15 nucleotides that can hybridize specifically to the polynucleotide of claim 4, but neither to a polynucleotide encoding SEQ ID NO: 11 nor to a polynucleotide encoding an amino acid sequence consisting of amino acids 1031 to 2517 of SEQ ID NO: 5.

24. (Reiterated) The oligonucleotide of claim 23, wherein the polynucleotide encodes at least five contiguous amino acids of a sequence selected from the group consisting of:

amino acids 720 to 745 of SEQ ID NO: 5;

amino acids 716 to 742 of SEQ ID NO: 7; and

amino acids 497 to 523 of SEQ ID NO: 9.

25. (Reiterated) The oligonucleotide of claim 23, which can hybridize specifically to a polynucleotide encoding SEQ ID NO: 5 or SEQ ID NO: 7, but not to a polynucleotide encoding SEQ ID NO: 9.

38. (Reiterated) A polynucleotide of claim 13, wherein said polynucleotide comprises nucleotides 1 to 7465 of SEQ ID NO: 8.